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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LAU, JONATHAN S	
ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
10/28/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/509,675	DEL SOLDATO, PIERO	
	Examiner	Art Unit	
	Jonathan S. Lau	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) *2, 5 and 6* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4 and 7-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12 Aug 2008 has been entered.

This application is the national stage entry of PCT/EP03/03183, filed 27 Mar 2003; and claims benefit of foreign priority document ITALY MI2002A00077, filed 11 Apr 2002. An English language translation of the foreign priority document is not currently of record.

Claims 1-9 are pending in the current application. Claims 2, 5 and 6, drawn to a nonelected species, are withdrawn.

Rejections Withdrawn

Applicant's Amendment, filed 01 July 2008, with respect to claims 1, 3, 4 and 7-9 are rejected under 35 U.S.C. 112, first paragraph for not enabling any person skilled in the art to use or make the invention commensurate in scope with these claims has been fully considered and is persuasive, as amended claims 1 and 9 do not recite preventing

degenerative effects on cartilaginoid matrix or relapses of degenerative effects on cartilaginoid matrix.

This rejection has been **withdrawn**.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 4 and 7-9 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 1 recites "...administering to a subject with arthritis an effective amount of one or more compounds or salts thereof..." Claims 3, 4 and 7-9 depend from claim 1 and incorporate all limitations therein.

The specification discloses chemical salts, such as examples of organic salts: oxalic, tartaric, maleic, succinic, citric, trifluoroacetic acids; and examples of inorganic salts: nitric, hydrochloric, sulphuric, phosphoric acids at page 25, paragraphs 2-3; and the usual excipients of pharmaceutical compositions at page 25, paragraph 5. However, claims 1, 3, 4 and 7-9 are directed to encompass any salts, which only correspond in some undefined way to specifically instantly disclosed chemicals. None of these salts meet the written description provision of 35 USC § 112, first paragraph, due to lacking

chemical structural information for what they are and because chemical salts are highly variant and encompass a myriad of possibilities. The specification provides insufficient written description to support the genus encompassed by the claim, and no limiting definition of a "salt" is provided other than the salt of an organic or inorganic acid at page 25, paragraph 1 and non-limiting examples at page 25, paragraphs 2-3.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of the above specifically disclosed chemical structures, the skilled artisan cannot envision the detailed chemical structure of the encompassed derivatives, analogs, etc., regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The chemical structure itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only the structurally defined chemical compounds, but not the full breadth of the claims, meet the written description provision of 35 USC § 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC § 112 is severable from its enablement provision. (See Vas-Cath at page 1115.)

The court of *In re Curtis* held that "a patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when… the evidence indicates ordinary artisans could not predict the operability … of any other species." (see *In re Curtis* 354 F.3d 1347, 69 USPQ2d 1274, Fed. Cir. 2004). The court of *Noelle v. Lederman* also pointed out that generic claim to anti-CD40CR Mabs lacked written description support because there was no description of anti-human or other species Mabs, and no description of human CD40CR antigen. The court further pointed out that attempt to "define an unknown by its binding affinity to another unknown" failed. See 355 F.3d 1343, 69 USPQ2d 1508, Fed. Cir. 2004.
Definition of the salt as the product salifiable with an organic or inorganic acid at page

25, paragraph 1 defines the salt by its production using an unknown organic or inorganic acid.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Amended Claims 1, 3, 4 and 7-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Armour et al. (Arthritis and Rheumatism, 2001, 44(9), p2185-2192, provided by applicant as reference AN in IDS filed 08 Oct 2004). Couchman et al. (Agents and Actions, 1986, 19(1/2), p116-122, cited in PTO-892) provides evidence of inherency of the function or mechanism of action of the treatment disclosed by Armour et al.

Armour et al. discloses HTC1026 or flurbiprofen nitroxylbutylester (page 2185, left column, lines 10-11), the elected species, administered in vivo using a mouse model of ovariectomy-induced bone loss (page 2185, left column, lines 16-17), a model that is a subject with arthritis. The Merck Index shows the structure of flurbiprofen (The Merck Index, of record). Armour et al. discloses flurbiprofen nitroxylbutylester may be used for treatment of arthritis, characterized by joint inflammation as well as periarticular and systemic bone loss (page 2185, right column, lines 8-12). Armour et al. discloses administration of flurbiprofen nitroxylbutylester by intraperitoneal injections in corn oil

(page 2186, right column, lines 7-9), anticipating parenteral administration disclosed in instant claim 8. Armour et al. discloses HCT1026 retains the anti-inflammatory and analgesic activity of the nonnitrosylated parent compound, flurbiprofen, and that said compound is useful in inflammatory diseases such as rheumatoid arthritis (page 2192, left column, paragraph 1).

Couchman et al. provides evidence that non-steroidal anti-inflammatory drugs (NSAID) significantly reduce cartilage degradation by acting upon the production of chondrocyte stimulating factors (page 116, abstract). Couchman et al. provides evidence that despite previous experiments with the NSAID such as flurbiprofen showing no effect on catabolin production (page 116, left column, paragraph 1) NSAIDs are found to decrease the chondrocyte stimulating effect evidence by glycosaminoglycan release, and NSAIDs previously found to have no effect consistently decreased cartilage degradation (page 120, right column, paragraphs 1-2).

Note that "reducing degeneration of the cartilaginoid matrix" is merely considered to be a new function or mechanism of action of a treatment, flurbiprofen nitroxylbutylester administered to a mouse model of ovariectomy-induced bone loss, a subject with arthritis. It has been settled that the claiming of a new function or unknown property which is inherently present in the prior art method will not make the claim patentable as set forth in the 102(b) rejection above.

Moreover, the mechanism of action of a treatment does not have a bearing on the patentability of the invention if the method steps, i.e., administering the same compound in the same amount to the same or similar patient population, are already

known even though Applicant has proposed or claimed the mechanism (e.g., reducing degeneration of the cartilaginoid matrix). Applicant's recitation of a new mechanism of action for the prior art method will not, by itself, distinguish the instant claims over the prior art teaching the same or substantially identical method steps. Mere recognition of latent properties in the prior art does not render novel an otherwise known invention. See *In re Wiseman*, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. *In re Baxter Travenol Labs*, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

It is noted that In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess the characteristic relied on" (205 USPQ 594, second column, first full paragraph).

Response to Applicant's Remarks:

Applicant's remarks, filed 12 Aug 2008, have been fully considered and are not persuasive.

Applicant remarks that Armour et al. merely discloses the effect of HCT1026 on osteoclast cells in bones, and does not disclose any effect of HCT1026 on chondrocytes (the cells found in cartilage), much less reducing the degenerative effects on cartilaginoid matrix as in the method of the presently claimed invention.

As recited above, "reducing degeneration of the cartilaginoid matrix" is merely considered to be a new function or mechanism of action of a treatment, flurbiprofen nitroxylbutylester administered to a mouse model of ovariectomy-induced bone loss, a subject with arthritis. It has been settled that the claiming of a new function or unknown property which is inherently present in the prior art method will not make the claim patentable as set forth in the 102(b) rejection above. Couchman et al. provides evidence that it is an inherent function that non-steroidal anti-inflammatory drugs (NSAID) significantly reduce cartilage degradation by acting upon the production of chondrocyte stimulating factors (page 116, abstract), and Armour et al. discloses HCT1026 retains the anti-inflammatory and analgesic activity of the nonnitrosylated parent compound, flurbiprofen.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Amended Claims 1 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Armour et al. (Arthritis and Rheumatism, 2001, 44(9), p2185-2192, provided by applicant as reference AN in IDS filed 08 Oct 2004) in view of Gabalawy et al. (Arthritis Res. 2002, 4 (suppl 3), pS297-S301, published 09 May 2002, cited in PTO-892). Couchman et al. (Agents and Actions, 1986, 19(1/2), p116-122, cited in PTO-892) provides evidence of inherency of the function or mechanism of action of the treatment disclosed by Armour et al.

Armour et al. discloses as above. Armour et al. discloses HCT1026 retains the anti-inflammatory and analgesic activity of the nonnitrosylated parent compound, flurbiprofen, and that said compound is useful in inflammatory diseases such as rheumatoid arthritis (page 2192, left column, paragraph 1).

Armour et al. does not specifically disclose the method wherein relapses of degeneration of the cartilaginoid matrix are reduced.

Gabalawy et al. teaches relapse of rheumatoid arthritis is almost predictable after withdrawal of the antirheumatic drugs currently used in clinical practice (page S299, left column, paragraph 3). Gabalawy et al. teaches sustained or ongoing therapy may be used to reduce the possibility of a relapse (page S300, left column, paragraph 1).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine Armour et al. in view of Gabalawy et al. Both Armour et al. and of Gabalawy et al. are drawn to drugs to treat rheumatoid arthritis. One of ordinary skill

would have been motivated to combine Armour et al. in view of Gabalawy et al. because Gabalawy et al. teaches antirheumatic drugs currently used in clinical practice can be applied in sustained or ongoing therapy to reduce the possibility of a relapse. Couchman et al. provides evidence of inherency of the function or mechanism of action of the treatment disclosed by Armour et al., and said function or mechanism of action is also inherent in the treatment taught by Armour et al. in view of Gabalawy et al.

Conclusion

No claim is found to be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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